Applicant: Katia Georgopoulos et al.

Serial No.: 09/019,348 Filed: February 5, 1998

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REMARKS

An application for change in correspondence address is enclosed herein.

Claims 18-44 are pending. Claims 18, 19, 22, 28, 29, 35, 40 and 43-44 have been amended. Claims 19, 28, 40 and 43-44 have been amended to correct a mistake in antecedent basis or to correct the unintentional omission of the word "wherein." The amendments to the claim are supported throughout the application as filed, e.g., at page 34, lines 5-29. No new matter has been added.

Claims 18-21, 25-28, 29-31, 35-39 and 42-44 are rejected under 35 U.S.C. §112, second paragraph, "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." The Examiner argues as follows.

Base claims 18, 29 and 35 are drawn to a method of obtaining an antibody to an antigen, however a required step of immunizing the animal to the antigen is missing and is a required step to practice the invention, making the claims indefinite.

Claims 18, 29 and 35 have been amended to clarify that the animal recited in the claims is immunized with an antigen. However, Applicants respectfully traverse the Examiner's above-quoted statement that a step of immunizing the animal is required. The present claims are directed to a method of obtaining an antibody. The method includes: providing an animal that (a) has a cell which is Aiolos deregulated and (b) is immunized with an antigen; and isolating an antibody against the antigen from the animal or from a hematopoietic cell derived from the animal. Applicants note that the antigen can be, e.g., an autoantigen, as provided in claims 21, 31 and 39 (and, e.g., in the specification at page 34, lines 5-29). As the Examiner is aware, an autoantigen is an endogenous antigen that stimulates the production of autoantibodies. Therefore, an animal having autoantibodies to an autoantigen is considered to be immmunized against the autoantigen even though the animal was not affirmatively inoculated with an antigen. Thus, it would be clear to one of ordinary skill in the art that an affirmative step of inoculating the animal with the antigen is not a required step to practice the method as recited in the base claims. In light of the specification and present claims, the scope of the claims would be clear to

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one of ordinary skill in the art. Therefore, Applicants respectfully request that this rejection be withdrawn.

Applicants submit that all the claims are now in condition for allowance. However, should the Examiner believe that the present amendment and response do not place the application in condition for allowance, the Examiner is respectfully requested to contact the undersigned by telephone to resolve any remaining issue.

Attached is a marked-up version of the changes being made by the current amendment.

Enclosed is a Petition for Extension of Time with the required fee. Please apply any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

Attorney's Docket No.: 10287-031001 / MGH 1001.3

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Version with markings to show changes made

In the claims:

Claims 18, 19, 22, 28, 29, 35, 40 and 43-44 have been amended as follows:

- 18. (Twice Amended) A method of obtaining an antibody, comprising: providing a mammal that (a) [having]has a cell which is Aiolos deregulated and (b) is immunized with an antigen [and having an antigen]; and isolating an antibody against the antigen from the [animal]mammal or from a hematopoietic cell derived from the [animal]mammal, to thereby obtain an antibody.
 - 19. (Amended) The method of claim 18, wherein the mammal is a mouse
- 20. (Reiterated) The method of claim 18, wherein the mammal is an Aiolos transgenic mouse.
 - 21. (Reiterated) The method of claim 18, wherein the antigen is an autoantigen.
- 22. (Amended) The method of claim 18, wherein the mammal is immunized with an alloantigen or xenoantigen [the antigen].
- 23. (Reiterated) The method of claim 22, wherein the antigen is poorly antigenic in wild type animals.
- 24. (Reiterated) The method of claim 22, wherein the antigen has at least 90% homology between the first and second species as determined using the ALIGN program with a PAM120 weight residue table, a gap length penalty of 12, and a gap penalty of 4 or using XBLAST with default parameters, wherein the first species is the animal which provides the antibody and the second species is the species which provides the antigen.
 - 25. (Reiterated) The method of claim 18, wherein the antibody is an IgG antibody.
- 26. (Reiterated) The method of claim 18, the mammal carries homozygous null mutations at the Aiolos gene.

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27. (Reiterated) The method of claim 18, the method further comprises isolating one or more hematopoietic cells from the mammal and isolating the antibody therefrom.

- 28. (Twice Amended) The method of claim 18, wherein the hematopoietic cell from the animal is fused with a second cell to provide a hybridoma and the antibody is isolated from the hybridoma.
- 29. (Twice Amended) A method of obtaining an antibody comprising: providing a mouse that (a) has [having] a cell which is homozygous for null or underexpressing mutations at the Aiolos locus and (b) is immunized with an antigen [having an antigen]; and

isolating an antibody against the antigen from the [animal]mouse, to thereby obtain an antibody.

- 30. (Reiterated) The method of claim 29, wherein the mouse is an Aiolos transgenic mouse.
 - 31. (Reiterated) The method of claim 29, wherein the antigen is an autoantigen.
- 32. (Amended) The method of claim 29, wherein the [mammal] mouse is immunized with an alloantigen or xenoantigen[the antigen].
- 33. (Reiterated) The method of claim 32, wherein the antigen is poorly antigenic in wild type animals.
- 34. (Reiterated) The method of claim 32, wherein the antigen has at least 90% homology between the first and second species as determined using the ALIGN program with a PAM120 weight residue table, a gap length penalty of 12, and a gap penalty of 4 or using XBLAST with default parameters, wherein the first species is the animal which provides the antibody and the second species is the species which provides the antigen.
 - 35. (Twice Amended) A method of obtaining a monoclonal antibody, comprising:

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cell, to thereby obtain an antibody.

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providing a mouse that (a) has [having] a cell which is homozygous for null or underexpressing mutations at the Aiolos locus and (b) is immunized with an antigen [an having an antigen];

isolating a hematopoietic cell from the [animal]mouse; and isolating an antibody against the antigen from the hematopoietic cell or a derivative of the

- 36. (Reiterated) The method of claim 35, wherein the derivative is a hybridoma.
- 37. (Reiterated) The method of claim 35, wherein the cell is a lymphocyte.
- 38. (Reiterated) The method of claim 35, wherein the mouse is an Aiolos transgenic mouse.
 - 39. (Reiterated) The method of claim 35, wherein the antigen is an autoantigen.
- 40. (Amended) The method of claim 35, wherein the [mammal]mouse is immunized with an alloantigen or xenoantigen[the antigen].
- 41. (Reiterated) The method of claim 35, wherein the antigen is poorly antigenic in wild type animals.
- 42. (Reiterated) The method of claim 18, wherein the mammal is homozygous for a deletion of exon 7 of the Aiolos gene or a portion thereof.
- 43. (Amended) The method of claim 29, wherein the [mammal]mouse is homozygous for a deletion of exon 7 of the Aiolos gene or a portion thereof.
- 44. (Amended) The method of claim 35, wherein the [mammal]mouse is homozygous for a deletion of exon 7 of the Aiolos gene or a portion thereof.